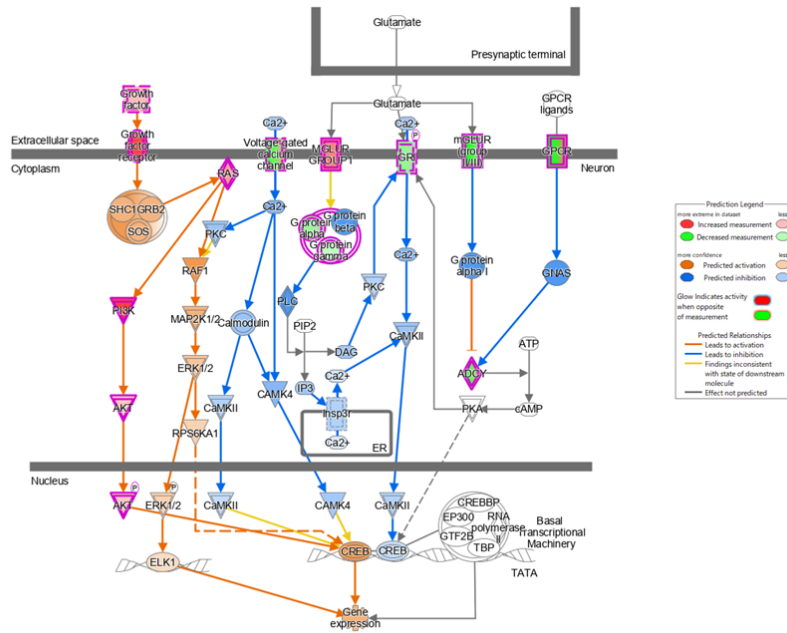
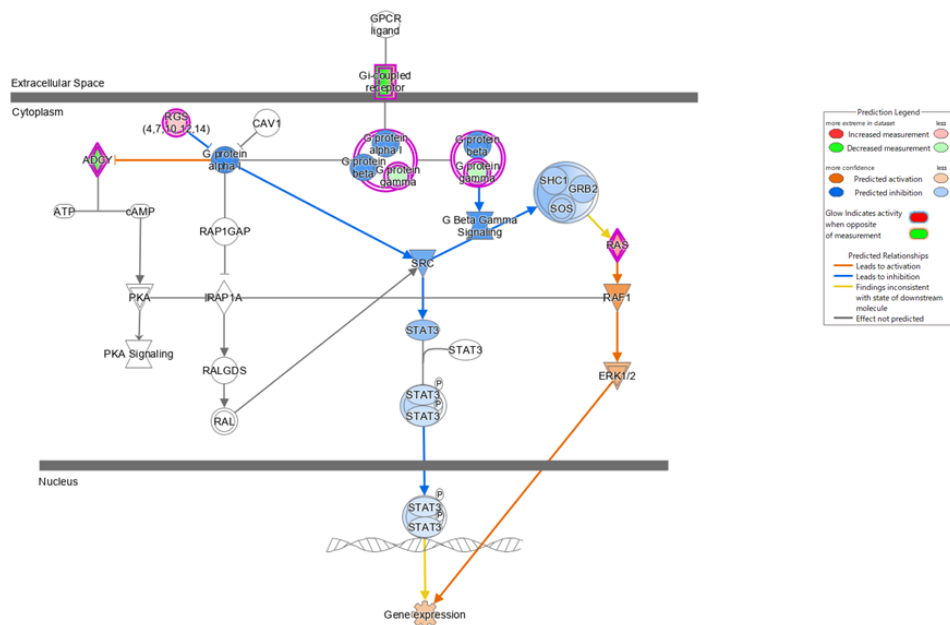


**Supplemental Figure S2 Canonical network of G-protein coupled receptor (GPCR) signaling**



Supplemental Figure S3 Canonical network of CREB signaling



Supplemental Figure S4 Canonical network of Gia mediated signaling

**Supplemental Table S1.** Sequence reads and mapping information of A549 Mock and A549 Rec.

Sample Name	Total reads	Trimmed Reads	Mapped reads	Mapping rate
A549_Rec1	35258092	34284440	33781100	98.53%
A549_Rec2	42631970	41192892	40546696	98.43%
A549_Rec	34299918	33567356	32962995	98.20%
A549_Mock1	36606010	35473726	34947741	98.52%
A549_Mock2	35675928	34243940	33723546	98.48%
A549_Mock	35126452	34364062	33782843	98.31%

**Supplemental Table S2.** List of the up-regulated or down-regulated DEGs (FDR adjusted  $p > 0.05$  and  $q < 0.08$ ) between A549 MOCK and A549 Rec.

gene_sym	log2FoldChange	p-value	q-value	Cellular_Component_Term	Molecular_Function_Term	Biological_Process_Term
RCVRN	14.73	<0.001	<0.001	perikaryon, dendrite, membrane, photoreceptor inner segment, photoreceptor outer segment,	calcium sensitive guanylate cyclase activator activity, calcium ion binding,	regulation of calcium ion transport, positive regulation of guanylate cyclase activity, phototransduction, visual perception, signal transduction,
KIFC1	5.04	>0.001	0.003	mitotic spindle, membrane, microtubule, kinesin complex, microtubule organizing center, early endosome, nucleus,	ATP hydrolysis activity, microtubule binding, ATP binding, microtubule motor activity,	mitotic spindle assembly, cell division, mitotic metaphase plate congression, microtubule-based movement, mitotic sister chromatid segregation,
ATF6B	4.71	0.002	0.005	RNA polymerase II transcription regulator complex, protein-DNA complex, Golgi apparatus, endoplasmic reticulum membrane, nucleus, chromatin,	sequence-specific double-stranded DNA binding, cAMP response element binding, protein binding, DNA-binding transcription factor activity, RNA polymerase II-specific, RNA polymerase II cis-regulatory region sequence-specific DNA binding,	ATF6-mediated unfolded protein response, endoplasmic reticulum unfolded protein response, signal transduction, regulation of transcription by RNA polymerase II,

				transcription cis-regulatory region binding,	
					regulation of renin secretion into blood stream, melanocyte proliferation, cellular response to fatty acid, detection of chemical stimulus
OR51E2	4.62	0.01	0.027	intracellular organelle, early endosome membrane, integral component of membrane, plasma membrane,	signaling receptor activity, olfactory receptor activity, G protein-coupled receptor activity, nuclear steroid receptor activity,
					involved in sensory perception of smell, regulation of blood pressure, regulation of cAMP-mediated signaling, steroid hormone mediated signaling pathway, melanocyte differentiation, cell migration, G protein-coupled receptor signaling pathway,
AC073911.3	4.55	0.015	0.026		
AC107959.2	4.47	0.018	0.028		
AP000240.1	4.3	0.037	0.042		
AP001625.2	4.28	0.033	0.04		
IL6R-AS1	4.1	0.01	0.023		
AC020663.1	4	0.013	0.024		
LENG8	3.79	<0.001	<0.001	protein-containing complex, nucleus,	protein binding,
BMS1P13	3.56	0.047	0.049		
ERMARD	3.55	0.001	0.005	integral component of membrane, endoplasmic reticulum membrane,	
AC027307.3	3.53	0.018	0.029		
					metal ion binding, protein binding, DNA-binding transcription factor activity, RNA polymerase II-specific, RNA polymerase II cis-regulatory
ZNF251	3.32	>0.001	0.002	nucleus,	hematopoietic stem cell homeostasis, regulation of transcription by RNA polymerase II,

					region sequence-specific DNA binding,	
DPH6-DT	3.1	0.038	0.043			
AC009065.3	2.76	0.024	0.032			
C4B-AS1	2.6	0.002	0.006			
						regulation of autophagosome assembly, extrinsic apoptotic signaling pathway in absence of ligand, apoptotic signaling pathway, regulation of release of cytochrome c from mitochondria, intrinsic apoptotic signaling pathway in response to DNA damage, extrinsic apoptotic signaling pathway via death domain receptors, autophagy, protein insertion into mitochondrial membrane involved in apoptotic signaling pathway,
MOAP1	2.44	0.009	0.024	cytosol, mitochondrial outer membrane, mitochondrion, cytoplasm,	ubiquitin protein ligase binding, protein binding,	
MRM1	2.41	<0.001	<0.001	mitochondrial matrix, mitochondrion,	rRNA (guanine) methyltransferase activity, protein binding, RNA binding,	rRNA 2'-O-methylation, rRNA modification,
SRMS	2.2	0.027	0.032	extrinsic component of cytoplasmic side of plasma membrane, cytosol, cytoplasm,	ATP binding, protein binding, signaling receptor binding, protein tyrosine kinase activity,	innate immune response, peptidyl-tyrosine autophosphorylation, cell differentiation, peptidyl-tyrosine phosphorylation, regulation of signal transduction, transmembrane receptor protein tyrosine kinase signaling pathway,
AC239859.6	2.18	0.02	0.03			

LRRC37A5 P	1.95	0.049	0.049			
					inositol-1,3,4-trisphosphate 5-kinase activity, inositol-1,3,4-trisphosphate 6-kinase activity, inositol	necroptotic process, inositol phosphorylation, inositol
ITPK1	1.68	<0.001	<0.001	apical plasma membrane, cytosol,	tetrakisphosphate 1-kinase activity, isomerase activity, inositol tetrakisphosphate 6-kinase activity, magnesium ion binding,	trisphosphate metabolic process, neural tube development, blood coagulation, signal transduction,
AC010643.1	1.31	0.034	0.04			
						regulation of anoikis, regulation of endothelial cell-matrix adhesion via fibronectin, regulation of heterotypic cell-cell adhesion, regulation of cell migration, regulation of cell population proliferation, signal transduction, heterophilic cell-cell adhesion via plasma membrane cell adhesion molecules, apoptotic process,
CEACAM6	1.28	<0.001	<0.001	azurophil granule membrane, anchored component of membrane, apical plasma membrane, cell surface, extracellular space,	protein heterodimerization activity, protein binding,	
AL359198.1	1.26	0.041	0.044			
GTF2IP1	1.22	0.021	0.03			
				eukaryotic 48S preinitiation complex, eukaryotic 43S preinitiation complex, eukaryotic translation initiation factor 3 complex, cytosol,	ribosome binding, translation initiation factor binding, protein binding, RNA binding,	regulation of mRNA binding, regulation of translation, translational initiation, formation of cytoplasmic translation initiation complex, cellular response to leukemia
EIF3C	1.16	0.012	0.025			
					histone binding, chromatin DNA binding,	inhibitory factor, osteoclast fusion, cellular response to lipopolysaccharide, bone trabecula
SBNO2	1.13	<0.001	<0.001	nucleus,		

						morphogenesis, regulation of inflammatory response, regulation of transcription by RNA polymerase II, regulation of DNA-templated transcription, osteoclast differentiation, bone mineralization, macrophage activation involved in immune response, response to sodium phosphate, biomineralization, leukotriene transport, transmembrane transport, calcium ion homeostasis, phosphate ion homeostasis, ATP metabolic process, response to magnesium ion, cellular phosphate ion homeostasis, inorganic diphosphate transport, ATP transport, gene expression, response to xenobiotic stimulus, visual perception,
ABCC6	1.02	0.014	0.029	basolateral plasma membrane, integral component of membrane, plasma membrane, endoplasmic reticulum membrane, nucleoplasm, extracellular region,	ATPase-coupled inorganic anion transmembrane transporter activity, ATPase-coupled transmembrane transporter activity, ABC-type glutathione S-conjugate transporter activity, ATP binding,	

gene_sym	log2FoldChange	p-value	q-value	Cellular_Component_Term	Molecular_Function_Term	Biological_Process_Term
IGSF23	-4.74	0.007	0.051	integral component of membrane,		
AC090673.1	-4.64	0.023	0.063			
ARR3	-4.53	0.032	0.056	synapse, cytoplasm, photoreceptor inner segment, photoreceptor outer segment,	phosphoprotein binding, protein binding, opsin binding, G protein-coupled receptor binding,	visual perception, signal transduction, G protein-coupled receptor internalization, regulation of protein phosphorylation,

AC007405.3	-4.38	0.021	0.06			
GPR158	-4.37	0.026	0.058	integral component of membrane, plasma membrane,	G protein-coupled receptor activity,	protein localization to plasma membrane, G protein-coupled receptor signaling pathway,
AL009178.3	-4.35	0.03	0.057			
AL590006.1	-4.3	>0.001	0.009			
AC096720.2	-4.24	0.034	0.051			
INTS9-AS1	-4.22	0.035	0.051			
AC007216.2	-4.1	0.042				
MAGED4B	-4.02	0.006	0.061	nucleus,	protein binding,	regulation of transcription by RNA polymerase II,
AC096751.2	-3.78	0.025	0.058			
AL512506.1	-3.68	0.036	0.049			
AC104113.1	-3.65	0.036	0.048			
CDC37P1	-3.08	0.039	0.049			
LINC02256	-3.05	0.02	0.064			
RN7SKP173	-2.99	0.046	0.048			
				Gemini of coiled bodies, perikaryon, neuron projection, cytoplasmic ribonucleoprotein granule, SMN-Sm protein complex, SMN complex, axon, Z disc, nuclear body, Cajal body, cytosol, cytoplasm, nucleoplasm nucleus,		
SMN2	-2.98	0.021	0.062		protein binding, RNA binding,	nervous system development, DNA- templated transcription termination, spliceosomal snRNP assembly, spliceosomal complex assembly,
SNORA71A	-2.86	0.024	0.059	nucleolus,		RNA processing,
LUNAR1	-2.83	0.01	0.057			
AP001992.1	-2.78	0.037	0.047			



UBR7	-2.69	0.019	0.07		ubiquitin protein ligase activity, zinc ion binding,	protein ubiquitination,
AC108448.3	-2.66	0.042	0.049			
AC067930.5	-2.53	0.049	0.049			
LY6E	-2.48	0.015	0.07	anchored component of membrane, plasma membrane, extracellular region,	acetylcholine receptor inhibitor activity, protein binding,	regulation of signaling receptor activity, regulation of viral entry into host cell, cell surface receptor signaling pathway,
AC011330.1	-2.39	>0.001	0.009			
SMIM11A	-2.33	0.007	0.054	integral component of membrane,	protein binding,	
AC009185.1	-2.27	0.033	0.052			
ZNF365	-2.25	0.043	0.048	centrosome, cytoplasm,	metal ion binding, protein binding,	dendrite arborization, regulation of DNA strand resection involved in replication fork processing, dendritic spine morphogenesis, regulation of oligodendrocyte differentiation, cerebellar molecular layer morphogenesis, regulation of neuron projection development, regulation of double-strand break repair via homologous recombination, telomere maintenance, telomere maintenance,
SPTIN5	-2.06	0.028	0.058	cell division site, septin complex, microtubule cytoskeleton, synaptic vesicle, septin ring, plasma membrane,	molecular adaptor activity, GTP binding, protein binding, structural molecule activity, GTPase activity,	regulation of synaptic vesicle exocytosis, cytoskeleton-dependent cytokinesis, social behavior, adult behavior, regulation of exocytosis,

						synaptic vesicle targeting, protein localization,
AL590644.1	-2.06	0.032	0.057	extracellular exosome, receptor complex, lysosomal lumen, microvillus membrane, brush border membrane, extrinsic component of external side of plasma membrane, endocytic vesicle, apical plasma membrane, clathrin-coated pit, cytosol, Golgi apparatus, endoplasmic reticulum, endosome, lysosomal membrane,		
CUBN	-2.05	0.033	0.053		protein homodimerization activity, cargo receptor activity, signaling receptor activity, cobalamin binding, protein binding, calcium ion binding,	establishment of localization in cell, lipoprotein transport, response to bacterium, cobalamin metabolic process, cholesterol metabolic process, receptor-mediated endocytosis, tissue homeostasis,
GCOM2	-2.02	0.036	0.048			
DHRS11	-1.97	0.003	0.032	extracellular region,	cycloeucalenone reductase activity, 17-beta-hydroxysteroid dehydrogenase (NADP+) activity, 17-beta-ketosteroid reductase activity, 17-beta-hydroxysteroid dehydrogenase (NAD+) activity, estradiol 17-beta-dehydrogenase activity, 3-keto sterol reductase activity, nucleotide binding,	estrogen biosynthetic process, steroid biosynthetic process,
NAPEPLD	-1.93	0.019	0.072	extracellular exosome, membrane-bounded organelle, photoreceptor outer segment membrane, Golgi apparatus, early endosome, cytoplasm,	N-acetylphosphatidylethanolamine-hydrolysing phospholipase activity, N-acylphosphatidylethanolamine-specific phospholipase D activity, protein binding, bile acid binding, zinc ion binding,	regulation of brown fat cell differentiation, N-acylphosphatidylethanolamine metabolic process, regulation of inflammatory response, host-mediated regulation of intestinal

				nucleoplasm, nuclear envelope, Golgi membrane,		microbiota composition, phospholipid catabolic process, temperature homeostasis, retinoid metabolic process, regulation of histone H3-K27 methylation, cellular response to DNA damage stimulus, regulation of DNA-templated transcription, chromatin organization,
PHF1	-1.93	0.035	0.05	site of double-strand break, centrosome, cytoplasm, nucleoplasm, nucleus,	histone methyltransferase binding, metal ion binding, methylated histone binding, protein binding, chromatin binding, DNA binding, transcription corepressor binding,	
AC134775.1	-1.8	0.032	0.063			
HERC2P8	-1.74	0.024	0.06			
				anchoring junction, collagen-containing extracellular matrix, synaptic cleft, neuromuscular junction, extracellular matrix, cell junction, plasma membrane, extracellular space, basement membrane, collagen trimer,		establishment of protein localization to membrane, skeletal muscle acetylcholine-gated channel clustering, extracellular matrix organization, regulation of synaptic assembly at neuromuscular junction, acetylcholine catabolic process in synaptic cleft,
COLQ	-1.74	0.03	0.057		heparin binding, protein binding, extracellular matrix structural constituent,	
				integral component of membrane,		
PRRT1B	-1.73	0.043	0.049			regulation of wound healing, regulation of cell death, bone development, regulation of inflammatory response, regulation of smooth muscle cell proliferation, regulation of fat cell differentiation, glucose homeostasis, regulation of Wnt signaling pathway, regulation
WISP1	-1.64	0.009	0.056	extracellular matrix, cytosol, extracellular space,	heparin binding, protein binding, integrin binding,	

						of smooth muscle cell migration, cell-cell signaling, signal transduction, cell adhesion, regulation of cytokine production, RNA processing, cell-cell adhesion via plasma- membrane adhesion molecules, cochlea development, protein localization to plasma membrane, condensed mesenchymal cell proliferation, digestive tract development, ossification involved in bone maturation, post-anal tail morphogenesis, hippo signaling, adherens junction organization, neurogenesis, neural tube development, pattern specification process, multicellular organism development, cell-cell junction assembly, cell migration involved in endocardial cushion formation, mitral valve formation, branching involved in ureteric bud morphogenesis, cell morphogenesis,
SNORA71C	-1.63	0.036	0.05	nucleolus,		
DCHS1	-1.6	0.038	0.048	apical part of cell, catenin complex, integral component of membrane, adherens junction,	cadherin binding, calcium ion binding,	
AGGF1P2	-1.57	0.046	0.049			
CCHCR1	-1.55	0.017	0.072	cytosol, centriole, nucleus,	protein binding,	cell differentiation, protein export from nucleus,
DTNA	-1.52	0.02	0.069	anchoring junction, synapse, intermediate filament	zinc ion binding, protein binding,	synaptic signaling, neuromuscular synaptic transmission, chemical

				cytoskeleton, protein-containing complex, cell junction, plasma membrane, cytoplasm, nucleoplasm,		synaptic transmission, striated muscle contraction,
						regulation of DNA-templated transcription initiation, regulation of intrinsic apoptotic signaling pathway, homeostasis of number of cells, fibroblast proliferation, regulation of DNA-templated transcription, ribosome biogenesis, cytoplasm organization, nucleolus organization, transcription initiation at RNA polymerase I promoter, in utero embryonic development, RNA polymerase I preinitiation complex assembly,
RRN3	-1.41	0.032	0.054	nucleus,	RNA polymerase I general transcription initiation factor activity, RNA polymerase I core promoter sequence-specific DNA binding, RNA polymerase I core binding,	ephrin receptor signaling pathway,
						axon guidance, multicellular organism development,
EPHA10	-1.34	0.002	0.026	receptor complex, neuron projection, plasma membrane, extracellular region,	ATP binding, protein binding, transmembrane-ephrin receptor activity, transmembrane receptor protein tyrosine kinase activity,	transmembrane receptor protein tyrosine kinase signaling pathway,
RASA4CP	-1.34	0.042	0.049			
AL672207.1	-1.33	0.045	0.05			
				integral component of		
STEAP1B	-1.26	0.028	0.059	membrane, plasma membrane, endosome,	protein binding,	
SDCCAG8	-1.24	>0.001	0.007	photoreceptor cell cilium, ciliary basal body, centriolar	protein binding,	regulation of cilium assembly, tube formation, microtubule organizing

				satellite, cell-cell junction, cytosol, centriole, centrosome,		center organization, cell projection organization, establishment of cell polarity, centrosome cycle, neuron migration,
C1DP1	-1.17	0.029	0.058			
						cellular response to amyloid-beta, regulation of ERK1 and ERK2 cascade, chemotaxis, regulation of phagocytosis, regulation of inflammatory response, regulation of innate immune response, defense response to bacterium, regulation of superoxide anion generation, calcium-mediated signaling, regulation of cytosolic calcium ion concentration, G protein-coupled receptor signaling pathway, cell surface receptor signaling pathway, cell adhesion, complement receptor mediated signaling pathway, regulation of protein phosphorylation,
FPR2	-1.12	0.046	0.049	ficolin-1-rich granule membrane, tertiary granule membrane, specific granule membrane, integral component of membrane, plasma membrane, cytoplasm,	signaling receptor activity, protein binding, scavenger receptor binding, N-formyl peptide receptor activity, G protein-coupled receptor activity, complement receptor activity, amyloid- beta binding,	
RPL17	-1.1	0.013	0.068	cytosolic ribosome, cytosol, cytoplasm, nucleus,	protein binding, structural constituent of ribosome, RNA binding,	translation, cytoplasmic translation,
AC138466.4	-1.07	0.024	0.055			
PHYHIP	-1.03	0.048	0.049	cytoplasm,	protein tyrosine kinase binding,	protein localization,